SYNTHESIS AND SOME PROPERTIES OF ETHYL 2-OXO-4-CYANO-1-OXASPIRO[4,5]DECANE-3-CARBOXYLATE

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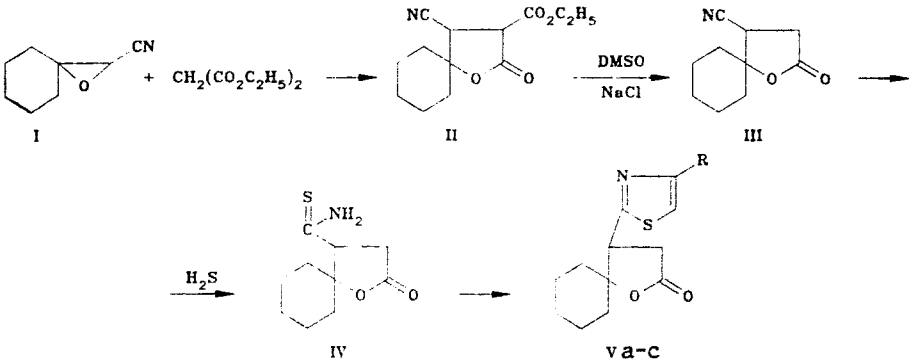
UDC 547.473.2+547.789.1

It was established by NMR and mass spectrometry that 1-oxaspiro[2,5]octane-2-carboxylic acid nitrile is converted, by the action of sodium malonate in toluene, to ethyl 2-oxo-4-cyano-1-oxaspiro[4,5]decane-3-carboxylate, which, upon refluxing in DMSO, is de-ethoxycarbonylated to give 2-oxo-1-oxaspiro[4,5]decane-4-carboxylic acid nitrile. The latter is converted to a thioamide, on the basis of which some thiazoles were synthesized.

We have recently established that in the reaction of ethyl 1-oxaspiro[2,5]-2-carboxylate with sodium malonate opening of the oxirane ring takes place exclusively at the α-C—O bond [1]. In the present research we have shown that the way in which the oxirane ring opens does not change in the reaction of 1-oxaspiro[2,5]octane-2-carboxylic acid nitrile (I) [2] with sodium malonate; the product is ethyl 2-oxo-4-cyano-1-oxaspiro[4,5]decane-3-carboxylate (II), the structure of which was proved by NMR and mass spectrometry. We also established that the protons in the 3 and 4 positions have a trans configuration.



V a R=C_6H_5; b R=*p*-Cl—C_6H_4; c R=*p*-NO_2—C_6H_4

Refluxing spirolactone II in DMSO in the presence of sodium chloride leads to de-ethoxycarbonylation to give 2-oxo-1-oxaspiro[4,5]decane-4-carboxylic acid nitrile (III), the addition of hydrogen sulfide to which gives thioamide IV. The reaction of the latter with some ω-bromo ketones was used to synthesize thiazoles V. Thus, for the first time, we have established that in nitrile I, as in ethyl 1-oxaspiro[2,5]octane-2-carboxylate (II) [1], the oxirane ring, under the influence of sodium malonate, opens up exclusively at the α-C—O bond.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil were recorded with a UR-20 spectrometer. The PMR spectra were obtained with a Varian T-60 spectrometer with tetramethylsilane (TMS) as the internal standard. The mass spectra were recorded with an MKh-1320 spectrometer with direct introduction of the samples into the ion source at an ionizing voltage of 70 eV. Thin-layer chromatography was carried out on Silufol UV-254 plates with development by iodine vapors.

The results of elementary analysis of II-V for C, H, N, and S were in agreement with the calculated values.

Ethyl 2-Oxo-4-cyano-1-oxaspiro[4,5]decane-3-carboxylate (II, $C_{13}H_{17}NO_4$). An 80.1-g (0.5 mole) sample of diethyl malonate was added gradually (in portions) at 60-70°C to 12.5 g (0.5 mole) of finely divided sodium in

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TABLE 1. Characteristics of Va-c

Compound	Empirical formula	mp,* °C	R_f*2	IR spectrum, cm^{-1}		PMR spectrum, δ, ppm ($CDCl_3$, TMS)	Mass spectrum, m/z (I, %)*3	Yield, %
				C=C arom.	C=O lact.			
Va	$C_{18}H_{19}NO_2S$	127	0,67	1500	1760	0,70...2,11 (10H, m, 6,7,8,9,10-CH_2); 2,60...3,19 (2H, m, 3-CH_2); 3,50 (1H, dd, 4-CH); 7,36 (1H, s, 5′-CH); 7,15...7,98 (5H, m, C_6H_5)	313 (10), 215 (62), 187 (100), 175 (3), 134 (57), 90 (6), 78 (3), 57 (13)	74,5
V	$C_{18}H_{18}ClNO_2S$	110	0,50	1490	1770	0,6...2,13 (10H, m, 6,7,8,9,10-CH_2); 2,63...3,36 (2H, m, 3-CH_2); 3,80 (1H, dd, 4-CH); 7,4 (1H, s, 5′-CH); 7,23...7,91 (4H, m, C_6H_4)	347*4 (23), 249*4 (64), 221*4 (100), 168*4 (23), 149 (5), 133 (5)	88
V	$C_{18}H_{18}N_2O_4S$	158	0,58	1500, 1600	1770	0,40...2,13 (10H, m, 6,7,8,9,10-CH_2); 2,75...3,35 (2H, m, 3-CH_2); 3,83 (1H, dd, 4-CH); 7,35 (1H, s, 5′-CH); 7,96...8,50 (4H, m, C_6H_4)	358 (9), 328 (5), 260 (100), 233 (17), 232 (95), 202 (19), 186 (10), 179 (5), 149 (9), 133 (3), 85 (9)	60

*1Compound Va was recrystallized from ether—hexane (1:1), while Vb, c were crystallized from ethanol.
*2The solvents used were as follows: chloroform—benzene (9:1) for Va, chloroform—acetone (98:2) for Vb, and chloroform—acetone (9:1) for Vc.
*3The peaks of ions with intensities ≥ 3% are presented (the intensities of the ions in percent of the molecular ion are presented in parentheses).
*4Ions containing the ^{35}Cl isotope.

200 ml of toluene, after which the mixture was stirred for 1 h, It was then treated with 34.3 g (0.25 mole) of nitrile I [2], and the mixture was refluxed for 25 h at 90°C. It was then cooled and acidified with 15% HCl. The organic layer was separated, the aqueous layer was extracted twice with ether, and the organic layer and the extracts were combined, washed with water, and dried with magnesium sulfate. Removal of the solvents by distillation gave a residue, which was distilled in vacuo at 192-197°C (2 hPa) to give a product with n_D^{20} 1.4695, d_4^{20} 1.4090, and R_f 0.59 [chloroform—acetone (9:1)]. IR spectrum: 1750 (ester C=O), 1790 (lactone C=O), 2260 cm^{-1} (C≡N). PMR spectrum (CCl_4): 1.33 (3H, t, J = 7 Hz, 3-$COOCH_2CH_3$), 1.58-2.15 (10H, m, 6,7,8,9,10-CH_2), 3.58 (1H, d, J = 11.5 Hz, 4-CH), 3.98 (1H, d, J = 11.5 Hz, 3-CH), 4.30 ppm (2H, q, J = 7 Hz, 3-$COOCH_2CH_3$). Mass spectrum, m/z (%): 251 (10), 233 (6), 223 (15), 205 (77), 187 (25), 179 (43), 178 (100), 165 (43), 162 (33), 153 (34), 122 (23), 107 (22), 99 (30), 81 (66). The yield was 43.9 g (70%).

2-Oxo-1-oxapyro[4,5]decane-4-carboxylic Acid Nitrile (III, $C_{10}H_{13}NO_2$). A mixture of 24.6 g (0.098 mole) of ethyl ester II, 12.25 g (0.35 mole) of sodium chloride, 6.6 1 ml of water, and 130 ml of DMSO was refluxed for 5 h, after which the DMSO was removed by distillation at reduced pressure, the residue was extracted with ether, and the ether extract was dried over magnesium sulfate. After removal of the ether by distillation, the residue was recrystallized from ethanol to give a product with mp 92-93°C and R_f 0.63 [chloroform—ethanol (9:1)]. IR spectrum: 1780 (lactone C=O), 2260 cm^{-1} (C≡N). PMR spectrum ($CDCl_3$): 1.16-2.25 (10H, m, 6,7,8,9,10-CH_2), 2.76-3.45 ppm (3H, m, 3-CH_2 and 4-CH). The yield was 10 g (60%).

2-Oxo-1-oxapyro[4,5]decane-4-carboxylic Acid Thioamide (IV, $C_{10}H_{15}NO_2S$). A dried (over calcium chloride) stream of hydrogen sulfide was passed with stirring and heating at 70-75°C in the course of 6 h through a mixture of 11.2 g (0.062 mole) of nitrile III, 42.5 ml of pyridine, and 14.5 ml of triethylamine, after which the reaction mixture was allowed to stand at room temperature for two days. After removal of the solvent by distillation, 40 ml of hexane was added, and the precipitated crystals of thioamide IV were removed by filtration and recrystallized from benzene to give a product with mp 215°C [chloroform—acetone (7:3)]. IR spectrum: 1630 (amide C=S); 1740 (lactone C=O); 3150, 3300 cm^{-1} (NH_2). PMR spectrum (d_6-pyridine): 0.63-2.50 (10H, m, 6,7,8,9,10-CH_2), 2.94 (1H, dd, 4-CH), 3.43-3.84 ppm (2H, m, 3-CH_2). The yield was 9 g (70%).

2-Oxo-4-(4′-substituted 2′-thiazolyl)-1-oxaspiro[4,5]decanes Va-c). A 0.02-mole sample of thioamide IV in 20 ml of acetone was added to a solution o 0.02 mole of ω-bromoacetophenones in 20 ml of absolute acetone. After 5-10 min, the thiazole hydrobromides began to precipitate. The reaction mixture was allowed to stand for 5 h, and the precipitated hydrobromide was removed by filtration, washed with ether, and treated with 15% sodium carbonate solution. The resulting mixture was extracted with ether, and the ether extract was dried over magnesium sulfate. After removal of the solvent by distillation, the resulting crystals were recrystallized from a suitable solvent (see Table 1).

LITERATURE CITED

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